Granulocytic Anaplasmosis in humans and animals

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Introduction

Granulocytic Anaplasmosis (GA) is an emerging infectious disease of humans and an established infectious disease of domestic animals. GA is spread by ticks that carry the bacterial agent *Anaplasma phagocytophilum*. Like many other tick-borne diseases, GA is officially a reportable disease in humans[1]. Current research is aimed at better understanding these tick-borne bacterial diseases, as they are progressively spreading throughout both the U.S. and the world.

Bacterial pathogen

Anaplasma phagocytophilum is a gram-negative bacterium in the family Anaplasmataceae in the order Rickettsiales[2] (figure 1). The genera *Anaplasma* and *Ehrlichia* are comprised of tick-borne bacteria that primarily infect host blood cells.

Figure 1.

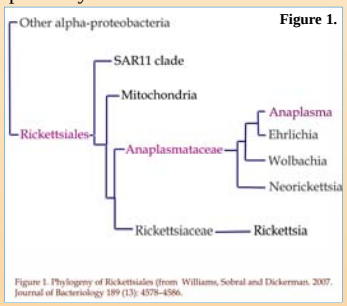


Figure 1. Phylogeny of Rickettsiales (from Williams, Sobral and Dickerman. 2007. Journal of Bacteriology 189 (13): 4578–4586.

A. phagocytophilum organisms infect neutrophils (the essential bacterial-killing cells of the immune system). This unusual strategy requires that the bacteria disable neutrophil killing mechanisms to permit their survival inside these cells. As the infected neutrophils freely circulate within the body, this survival strategy provides *A. phagocytophilum* the means to disseminate throughout the host human or animal and establish a nidus of infection (often the spleen).

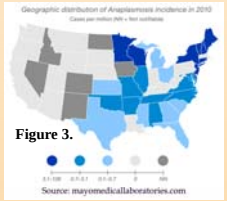
Tick vector

GA is vectored by several species of the *Ixodes* tick genus in the Ixodidae family of hard-bodied ticks (figure 2).

Figure 2.

Ixodes spp. ticks transmit a number of infectious diseases to humans and animals. In the U.S., GA is vectored by *Ixodes scapularis* in the Midwest and Northeast, and by *Ixodes pacificus* on the West coast (figure 3). These same tick species carry and transmit Lyme disease in these locations, along with a parasitic infection called babesiosis. Disease transmission generally takes at least one day following tick attachment. Tick ranges will likely expand in the future due to land use increase and climate change, raising concern for increased spread of tick-borne diseases. Preventing tick exposure will become increasingly important in controlling the spread of diseases.

Figure 3.



Animal reservoirs

Animals reservoirs of GA in many parts of the U.S. include the white-footed mouse (*Peromyscus leukopus*; figure 4) and white-tailed deer (*Odocoileus virginianus*; figure 5). On the west coast, the dusky-footed woodrat (*Neotoma fuscipes*) and the western grey squirrel (*Sciurus griseus*) are reservoirs of GA infection. The relative importance of each animal reservoir in the spread of GA is still under investigation[3].

Figure 4.

Figure 5.

Disease in animals

GA is a well-known disease of livestock, with reports of this "tick-borne fever" dating back more than 200 years. Small ruminants, horses and dogs most commonly develop GA. Clinical signs in animals include fever, lethargy and lameness; horses additionally develop limb edema and mucosal petechiation[4].

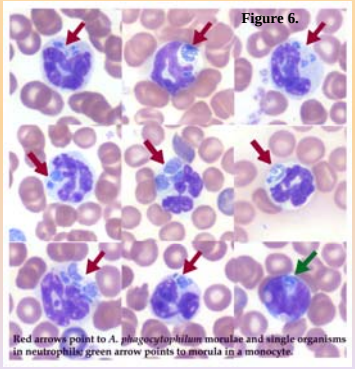
Disease in humans

In contrast to GA in animals, the first human case of GA was only reported in 1994. The first report in Europe soon followed. The symptoms of GA in humans are similar to clinical signs in animals and include fever, malaise, headache and muscle pain. Respiratory and gastrointestinal symptoms may develop. About 40-50% of human GA patients will require hospitalization and 7% will require intensive care[5].

Diagnosis and treatment

Hematologic abnormalities in GA include thrombocytopenia, the single most common finding in animals and humans. Morulae (clusters of bacteria) may be found in neutrophils in the blood smear (figure 6). Serology can be useful for diagnosis but cross-reactivity with *Ehrlichia* species can necessitate the use of PCR to confirm infection[6]. The standard treatment is doxycycline.

Figure 6.



Prevention

Ticks are most active between April and September, so prevention is most important during these months. While outdoors, people should avoid thick brush, apply repellants to clothing (or use pre-treated clothing and outdoor gear) and use tick preventatives on pets. Prompt removal of ticks is also vital, to disease prevention. Drying clothes on high heat for up to an hour will kill any ticks that remain[1].

Current research

Because *A. phagocytophilum* is an obligate intracellular bacterium, it cannot survive outside of cells. A white blood cell-based 'cell line' (figure 7) is needed to maintain the bacteria in culture for research. Current work focuses on defining the mechanisms by which the bacteria are able to perturb the host immune response, such as altered production of neutrophils and other immune cells[7]. The key immune system regulators in GA differ from those for "typical" gram-negative infections, supporting the current concept of a unique host immune response to the tick-borne bacteria.

Figure 7.

References

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